#7



SEQUENCE LISTING

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<120> HEREGULIN VARIANTS

<130> 402E-476112US

<140> US 10/082,747

<141> 2002-02-22

<150> US 09/101,544

<151> 1998-07-17

<150> PCT/US/98/01579

<151> 1998-02-10

<150> US 08/799,054

<151> 1997-02-10

<160> 116

<170> FastSEQ for Windows Version 3.0

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<213> Homo sapiens

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Leu Cys Lys Cys Pro Asn Glu Phe Thr Gly Asp Arg Cys Gln Asn Tyr
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                            40
Val Met Ala Ser Phe Tyr Lys His Leu Gly Ile Glu Phe Met Glu Ala
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                                            60
Glu Glu Leu Tyr Gln Lys Arg
65
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Ser His Leu Val Lys Cys Ala Glu Lys Glu Lys Thr Phe Cys Val Asn
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Gly Glu Cys Phe Met Val Lys Asp Leu Ser Asn Pro Ser Arg Tyr
            20
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Leu Cys Lys Cys Gln Pro Gly Phe Thr Gly Ala Arg Cys Thr Glu Asn
        35
                            40
                                                45
Val Pro Met Lys Val Gln Asn Gln Glu Lys Ala Glu Glu Leu Tyr Gln
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                                            60
Lys Arg
65
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Ser His Leu Val Lys Cys Ala Glu Lys Glu Lys Thr Phe Cys Val Asn
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Gly Glu Cys Phe Met Val Lys Asp Leu Ser Asn Pro Ser Arg Tyr
            20
Leu Cys Lys Cys Pro Asn Glu Phe Thr Gly Asp Arg Cys Gln Asn Tyr
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                            40
Val Met Ala Ser Phe Tyr Lys Ala Glu Glu Leu Tyr Gln Lys Arg
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                        55
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<213> Homo sapiens <400> 4 Ser His Leu Val Lys Cys Ala Glu Lys Glu Lys Thr Phe Cys Val Asn 10 Gly Glu Cys Phe Met Val Lys Asp Leu Ser Asn Pro Ser Arg Tyr 25 Leu Cys Lys Cys Pro Asn Glu Phe Thr Gly Asp Arg Cys Gln Asn Tyr 35 40 45 Val Met Ala Ser Phe Tyr Ser Thr Ser Thr Pro Phe Leu Ser Leu Pro 50 55 60 Glu 65 <210> 5 <211> 66 <212> PRT <213> Rattus rattus <400> 5 Ser His Leu Ile Lys Cys Ala Glu Lys Glu Lys Thr Phe Cys Val Asn Gly Gly Glu Cys Phe Thr Val Lys Asp Leu Ser Asn Pro Ser Arg Tyr 20 30 Leu Cys Lys Cys Gln Pro Gly Phe Thr Gly Ala Arg Cys Thr Glu Asn Val Pro Met Lys Val Gln Thr Gln Glu Lys Ala Glu Glu Leu Tyr Gln 50 55 60 Lys Arg 65 <210> 6 <211> 71 <212> PRT <213> Rattus rattus <400> 6 Ser His Leu Ile Lys Cys Ala Glu Lys Glu Lys Thr Phe Cys Val Asn 1 10 15 Gly Glu Cys Phe Thr Val Lys Asp Leu Ser Asn Pro Ser Arg Tyr

<212> PRT

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Leu Cys Lys Cys Pro Asn Glu Phe Thr Gly Asp Arg Cys Gln Asn Tyr
Val Met Ala Ser Phe Tyr Lys His Leu Gly Ile Glu Phe Met Glu Ala
                        55
                                            60
Glu Glu Leu Tyr Gln Lys Arg
65
                    70
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      <400> 7
Ser His Leu Ile Lys Cys Ala Glu Lys Glu Lys Thr Phe Cys Val Asn
                                    10
Gly Glu Cys Phe Thr Val Lys Asp Leu Ser Asn Pro Ser Arg Tyr
            20
                                25
Leu Cys Lys Cys Pro Asn Glu Phe Thr Gly Asp Arg Cys Gln Asn Tyr
                            40
Val Met Ala Ser Phe Tyr Lys Ala Glu Glu Leu Tyr Gln Lys Arg
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Ser His Leu Ile Lys Cys Ala Glu Lys Glu Lys Thr Phe Cys Val Asn
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Gly Glu Cys Phe Thr Val Lys Asp Leu Ser Asn Pro Ser Arg Tyr
            20
                                25
                                                    30
Leu Cys Lys Cys Gln Pro Gly Phe Thr Gly Ala Arg Cys Thr Glu Asn
                            40
Val Pro Met Phe Tyr Ser Thr Ser Thr Pro Phe Leu Ser Leu Pro Glu
    50
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     <213> Rattus rattus
     <400> 9
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Ser His Leu Ile Lys Cys Ala Glu Lys Glu Lys Thr Phe Cys Val Asn
                                    10
Gly Glu Cys Phe Thr Val Lys Asp Leu Ser Asn Pro Ser Arg Tyr
            20
                                25
Leu Cys Lys Cys Gln Pro Gly Phe Thr Gly Ala Arg Cys Thr Glu Asn
                            40
                                                45
Val Pro Met Phe Tyr Ser Met Thr Ser Arg Arg Lys Arg Gln Glu Thr
                        55
Glu Lys Pro Leu Glu Arg Lys Leu Phe His Ser Leu Val Lys Glu Ser
                    70
                                        75
Lys
      <210> 10
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      <213> Homo sapiens
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Ser His Leu Val Lys Cys Ala Glu Lys Glu Lys Thr Phe Cys Val Asn
                 5
                                    10
Gly Glu Cys Phe Met Val Lys Asp Leu Ser Asn Pro Ser Arg Tyr
            20
                                25
Leu Cys Lys Cys Pro Asn Glu Phe Thr Gly Asp Arg Cys Gln Asn Tyr
        35
                            40
                                                45
Val Met Ala Ser Phe Tyr Ser Thr Ser Thr Pro Phe Leu Ser Leu Pro
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Glu
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Ser His Leu Val Lys Cys Ala Glu Lys Glu Lys Thr Phe Cys Val Asn
                                    10
Gly Glu Cys Phe Met Val Lys Asp Leu Ser Asn Pro Ser Arg Tyr
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Leu Cys Lys Cys Pro Asn Glu Phe Thr Gly Asp Arg Cys Gln Asn Tyr

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Val Met Ala Ser Phe Tyr Ser Thr Ser Thr Pro Phe Leu Ser Leu Pro
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Glu
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Ser His Leu Val Lys Cys Ala Glu Lys Glu Lys Thr Phe Cys Val Asn
                 5
Gly Glu Cys Phe Met Val Lys Asp Leu Ser Asn Pro Ser Arg Tyr
            20
                                 25
Leu Cys Lys Cys Pro Asn Glu Phe Thr Gly Asp Arg Cys Gln Asn Tyr
                             40
                                                 45
Val Met Ala Ser Phe Tyr Ser Thr Ser Thr Pro Phe Leu Ser Leu Pro
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                        55
                                             60
Glu
65
      <210> 13
      <211> 71
      <212> PRT
      <213> Gallus domesticus
      <400> 13
Ser His Leu Thr Lys Cys Asp Ile Lys Gln Lys Ala Phe Cys Val Asn
                                    10
Gly Gly Glu Cys Tyr Met Val Lys Asp Leu Pro Asn Pro Pro Arg Tyr
            20
                                25
                                                     30
Leu Cys Lys Cys Pro Asn Glu Phe Thr Gly Asp Arg Cys Gln Asn Tyr
                            40
                                                 45
Val Met Ala Ser Phe Tyr Lys His Leu Gly Ile Glu Phe Met Glu Ala
    50
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                                             60
Glu Glu Leu Tyr Gln Lys Arg
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                    70
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      <211> 49
      <212> PRT
      <213> Artificial Sequence
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<220>
     <223> Variant of the human heregulin-beta1 EGF-like domain
     containing a deletion of human heregulin-betal residues
     202-204
     <400> 14
Ser His Leu Val Lys Cys Ala Glu Lys Glu Lys Thr Phe Cys Val Asn
                 5
                                    10
Gly Glu Cys Phe Met Val Lys Asp Pro Ser Arg Tyr Leu Cys Lys
            20
                                25
Cys Pro Asn Glu Phe Thr Gly Asp Arg Cys Gln Asn Tyr Val Met Ala
                                                45
                            40
Ser
     <210> 15
     <211> 48
     <212> PRT
     <213> Homo sapiens
     <400> 15
Asn Ser Asp Ser Glu Cys Pro Leu Ser His Asp Gly Tyr Cys Leu His
                                    10
Asp Gly Val Cys Met Tyr Ile Glu Ala Leu Asp Lys Tyr Ala Cys Asn
            20
                                25
Cys Val Val Gly Tyr Ile Gly Glu Arg Cys Gln Tyr Arg Asp Leu Arg
                            40
        35
                                                45
     <210> 16
     <211> 49
      <212> PRT
      <213> Artificial Sequence
     <220>
     <223> Variant of the human heregulin-betal EGF-like domain
      <400> 16
Ser His Leu Val Lys Cys Ala Glu Lys Glu Lys Thr Phe Cys Val Asn
                 5
                                    10
                                                        15
1
Gly Glu Cys Phe Met Val Lys Asp Pro Ser Arg Tyr Leu Cys Lys
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35
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                                                 45
Ser
      <210> 17
      <211> 52
      <212> PRT
      <213> Artificial Sequence
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      <223> Variant of the human heregulin-betal EGF-like domain
      <400> 17
Trp Glu Leu Val Pro Cys Gly Trp Asp Arg Glu Gly Phe Cys Val Asn
                                     10
Gly Glu Cys Phe Met Val Lys Asp Leu Ser Asn Pro Ser Arg Tyr
            20
                                25
Leu Cys Lys Cys Pro Asn Glu Phe Thr Gly Asp Arg Cys Gln Asn Tyr
        35
                             40
                                                 45
Val Ile Ala Ser
    50
      <210> 18
      <211> 49
      <212> PRT
      <213> Artificial Sequence
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      <223> Variant of the human heregulin-beta1 EGF-like domain
      <400> 18
Trp Glu Leu Val Pro Cys Ala Glu Lys Glu Lys Thr Phe Cys Val Asn
                                    10
Gly Glu Cys Tyr Lys Val Arg Ile Tyr Gly Tyr Leu Met Cys Lys
            20
                                25
                                                     30
Cys Pro Asn Glu Phe Thr Gly Asp Arg Cys Gln Asn Tyr Val Ile Ala
        35
                            40
                                                 45
Ser
      <210> 19
      <211> 49
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Cys Pro Asn Glu Phe Thr Gly Asp Arg Cys Gln Asn Tyr Val Ile Ala

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<213> Artificial Sequence
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      <223> Variant of the human heregulin-betal EGF-like domain
      <400> 19
Trp Glu Leu Val Pro Cys Gly Trp Asp Arg Glu Gly Phe Cys Val Asn
                 5
                                    10
Gly Glu Cys Tyr Lys Val Arg Ile Tyr Gly Tyr Leu Met Cys Lys
Cys Pro Asn Glu Phe Thr Gly Asp Arg Cys Gln Asn Tyr Val Ile Ala
                            40
                                                45
Ser
      <210> 20
      <211> 49
      <212> PRT
      <213> Artificial Sequence
      <220>
      <223> Variant of the human heregulin-beta1 EGF-like domain
      <400> 20
Trp Glu Leu Val Pro Cys Gly Trp Asp Arg Glu Gly Phe Cys Val Asn
                                    10
Gly Glu Cys Tyr Lys Val Arg Ile Tyr Arg Tyr Arg Met Cys Lys
            20
                                25
Cys Pro Asn Glu Phe Thr Gly Asp Arg Cys Gln Asn Tyr Val Ile Ala
        35
                            40
                                                45
Ser
      <210> 21
      <211> 49
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     <213> Artificial Sequence
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     <223> Variant of the human heregulin-betal EGF-like domain
     <400> 21
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<212> PRT

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Ser His Leu Val Lys Cys Ala Glu Lys Glu Lys Thr Phe Cys Val Asn
 1
                 5
                                                         15
                                    10
Gly Gly Glu Cys Phe Met Val Lys Asp Tyr Gly Tyr Leu Met Cys Lys
            20
                                25
Cys Pro Asn Glu Phe Thr Gly Asp Arg Cys Gln Asn Tyr Val Ile Ala
                            40
                                                 45
Ser
      <210> 22
      <211> 52
      <212> PRT
      <213> Artificial Sequence
      <220>
      <223> Variant of the human heregulin-beta1 EGF-like domain
      <400> 22
Ser His Leu Val Lys Cys Gly Glu Glu Arg Glu Gly Phe Cys Val Asn
                                    10
Gly Glu Cys Tyr Arg Val Lys Thr Leu Ser Asn Pro Ser Arg Tyr
            20
                                25
                                                     30
Leu Cys Lys Cys Pro Asn Glu Phe Thr Gly Asp Arg Cys Gln Asn Tyr
        35
                            40
                                                 45
Val Met Ala Ser
    50
      <210> 23
      <211> 49
      <212> PRT
      <213> Artificial Sequence
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      <223> Variant of the human heregulin-beta1 EGF-like domain
      <400> 23
Ser His Leu Val Lys Cys Gly Glu Glu Arg Glu Gly Phe Cys Val Asn
Gly Glu Cys Phe Met Val Lys Asp Tyr Gly Tyr Leu Met Cys Lys
            20
                                25
                                                     30
Cys Pro Asn Glu Phe Thr Gly Asp Arg Cys Gln Asn Tyr Val Met Ala
        35
                            40
                                                 45
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Ser

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<210> 24
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      <213> Artificial Sequence
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      <223> Variant of the human heregulin-beta1 EGF-like domain
      <400> 24
Ser His Leu Val Lys Cys Gly Glu Glu Arg Glu Gly Phe Cys Val Asn
                                    10
Gly Glu Cys Tyr Arg Val Lys Thr Tyr Gly Tyr Leu Met Cys Lys
            20
                                25
Cys Pro Asn Glu Phe Thr Gly Asp Arg Cys Gln Asn Tyr Val Met Ala
                            40
Ser
      <210> 25
      <211> 52
      <212> PRT
      <213> Artificial Sequence
      <220>
      <223> Variant of the human heregulin-betal EGF-like domain
      <400> 25
Ser His Leu Val Lys Cys Gly Glu Glu Arg Glu Gly Phe Cys Val Asn
                                    10
Gly Glu Cys Phe Met Val Lys Asp Leu Ser Asn Pro Ser Arg Tyr
            20
                                25
                                                    30
Leu Cys Lys Cys Pro Asn Glu Phe Thr Gly Asp Arg Cys Gln Asn Tyr
                                                45
Val Ile Ala Ser
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      <210> 26
      <211> 49
      <212> PRT
      <213> Artificial Sequence
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C'

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Ser His Leu Val Lys Cys Ala Glu Lys Glu Lys Thr Phe Cys Val Asn

<400> 28

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1

10

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Gly Gly Glu Cys Tyr Arg Val Lys Thr Leu Ser Asn Pro Ser Arg Tyr
            20
                                                     30
Leu Cys Lys Cys Pro Asn Glu Phe Thr Gly Asp Arg Cys Gln Asn Tyr
        35
                            40
                                                 45
Val Ile Ala Ser
    50
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      <211> 52
      <212> PRT
      <213> Artificial Sequence
      <220>
      <223> Variant of the human heregulin-beta1 EGF-like domain
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Ser His Leu Val Lys Cys Gly Glu Glu Arg Glu Gly Phe Cys Val Asn
                 5
                                    10
                                                         15
 1
Gly Glu Cys Tyr Arg Val Lys Thr Leu Ser Asn Pro Ser Arg Tyr
            20
                                25
Leu Cys Lys Cys Pro Asn Glu Phe Thr Gly Asp Arg Cys Gln Asn Tyr
        35
                            40
                                                 45
Val Ile Ala Ser
    50
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      <212> PRT
      <213> Artificial Sequence
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      <400> 30
Ser His Leu Val Lys Cys Gly Glu Glu Arg Glu Gly Phe Cys Val Asn
                 5
1
                                    10
                                                         15
Gly Glu Cys Phe Met Val Lys Asp Tyr Gly Tyr Leu Met Cys Lys
                                25
Cys Pro Asn Glu Phe Thr Gly Asp Arg Cys Gln Asn Tyr Val Ile Ala
        35
                            40
                                                 45
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Ser

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<210> 31
      <211> 49
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      <213> Artificial Sequence
      <220>
      <223> Variant of the human heregulin-betal EGF-like domain
      <400> 31
Ser His Leu Val Lys Cys Gly Glu Glu Arg Glu Gly Phe Cys Val Asn
                                    10
Gly Glu Cys Tyr Arg Val Lys Thr Tyr Gly Tyr Leu Met Cys Lys
            20
                                25
Cys Pro Asn Glu Phe Thr Gly Asp Arg Cys Gln Asn Tyr Val Ile Ala
        35
                            40
                                                 45
Ser
      <210> 32
      <211> 49
      <212> PRT
      <213> Artificial Sequence
      <220>
      <223> Variant of the human heregulin-betal EGF-like domain
      <400> 32
Ser His Leu Val Lys Cys Ala Glu Lys Glu Lys Thr Phe Cys Val Asn
                                    10
                                                        15
Gly Glu Cys Tyr Arg Val Lys Thr Tyr Gly Tyr Leu Met Cys Lys
Cys Pro Asn Glu Phe Thr Gly Asp Arg Cys Gln His Tyr Val Ile Ala
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                                                45
Ser
     <210> 33
     <211> 49
     <212> PRT
     <213> Artificial Sequence
     <220>
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<223> Variant of the human heregulin-beta1 EGF-like domain

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<400> 33
Ser His Leu Val Lys Cys Gly Glu Glu Arg Glu Gly Phe Cys Val Asn
                                     10
                 5
Gly Glu Cys Tyr Arg Val Lys Thr Tyr Gly Tyr Leu Met Cys Lys
                                                     30
            20
Cys Pro Asn Glu Phe Thr Gly Asp Arg Cys Gln His Tyr Val Ile Ala
                                                 45
                            40
        35
Ser
      <210> 34
      <211> 4
      <212> PRT
      <213> Artificial Sequence
      <220>
      <223> Repeat sequence in linker joining human heregulin-
      betal residues 177-228 to M13 pIII residue 323
      <400> 34
Gly Gly Gly Ser
 1
      <210> 35
      <211> 7
      <212> PRT
      <213> Artificial Sequence
      <220>
      <223> Linker joining human heregulin-betal residues 177-230
      to M13 pIII residue 247
      <400> 35
Gly Gly Gly Ser Gly Gly Gly
                 5
 1
      <210> 36
      <211> 5
      <212> PRT
      <213> Artificial Sequence
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<220>

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<223> Linker for ERbB-2 receptor-immunoglobulin fusion
     proteins
      <400> 36
Thr Arg Asp Lys Thr
     <210> 37
     <211> 5
     <212> PRT
      <213> Artificial Sequence
     <220>
      <223> Enterokinase protease recognition site
     <400> 37
Asp Asp Asp Lys
 1
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     <210> 38
     <211> 5
     <212> PRT
     <213> Homo sapiens
      <400> 38
Ser His Leu Val Lys
 1
     <210> 39
     <211> 5
     <212> PRT
      <213> Artificial Sequence
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      <223> Variant sequence at human heregulin-beta1
      residues 177-181
     <400> 39
Trp Arg Leu Val Pro
1
                 5
     <210> 40
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<211> 5

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<212> PRT
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      <223> Variant sequence at human heregulin-beta1
      residues 177-181
      <400> 40
Trp Ser Leu Gln Pro
                 5
1
     <210> 41
     <211> 5
      <212> PRT
     <213> Artificial Sequence
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      <223> Variant sequence at human heregulin-beta1
      residues 177-181
      <400> 41
Trp Glu Leu Val Pro
1
                 5
     <210> 42
     <211> 5
      <212> PRT
      <213> Artificial Sequence
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      residues 177-181
      <400> 42
Trp Ser Leu Val Lys
1
                 5
     <210> 43
     <211> 5
      <212> PRT
      <213> Artificial Sequence
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<220>

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      residues 177-181
      <400> 43
Trp Ser Leu Ile Pro
      <210> 44
      <211> 5
      <212> PRT
      <213> Artificial Sequence
      <220>
      <223> Variant sequence at human heregulin-beta1
      residues 177-181
      <400> 44
Trp Arg Leu Val Ala
 1
                 5
      <210> 45
      <211> 5
      <212> PRT
      <213> Artificial Sequence
      <220>
      <223> Variant sequence at human heregulin-beta1
      residues 177-181
      <400> 45
Trp Ala Leu Val Pro
 1
      <210> 46
      <211> 5
      <212> PRT
      <213> Artificial Sequence
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      <223> Variant sequence at human heregulin-beta1
      residues 177-181
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<400> 46

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Trp Ser Leu Gln Lys
                  5
 1
      <210> 47
      <211> 5
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      <213> Artificial Sequence
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      <223> Variant sequence at human heregulin-beta1
      residues 177-181
      <400> 47
Trp Glu Leu Val Ala
 1
                 5
      <210> 48
      <211> 5
      <212> PRT
      <213> Artificial Sequence
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      <223> Variant sequence at human heregulin-beta1
      residues 177-181
      <400> 48
Trp Ser Leu Glu Pro
      <210> 49
      <211> 6
      <212> PRT
      <213> Homo sapiens
      <400>, 49
Ala Glu Lys Glu Lys Thr
 1
                 5
      <210> 50
      <211> 6
      <212> PRT
      <213> Artificial Sequence
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<220>
      <223> Variant sequence at human heregulin-betal
      residues 183-188
      <400> 50
Gly Val Gly Arg Asp Gly
 1
      <210> 51
      <211> 6
      <212> PRT
      <213> Artificial Sequence
      <220>
      <223> Variant sequence at human heregulin-beta1
      residues 183-188
      <400> 51
Gly Gly Glu Arg Glu Gly
      <210> 52
      <211> 6
      <212> PRT
      <213> Artificial Sequence
      <220>
      <223> Variant sequence at human heregulin-beta1
      residues 183-188
      <400> 52
Gly Glu Glu Arg Glu Gly
 1
      <210> 53
      <211> 6
      <212> PRT
      <213> Artificial Sequence
      <220>
      <223> Variant sequence at human heregulin-beta1
      residues 183-188
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<400> 53
Gly Trp Asp Arg Glu Gly
                 5
 1
      <210> 54
      <211> 6
      <212> PRT
      <213> Artificial Sequence
      <220>
      <223> Variant sequence at human heregulin-beta1
      residues 183-188
      <400> 54
Gly Val Gln Arg Glu Gly
                 5
      <210> 55
      <211> 6
      <212> PRT
      <213> Artificial Sequence
      <220>
      <223> Variant sequence at human heregulin-beta1
      residues 183-188
      <400> 55
Gly Glu Glu Arg Ala Gly
                  5
 1
      <210> 56
      <211> 6
      <212> PRT
      <213> Artificial Sequence
      <220>
      <223> Variant sequence at human heregulin-beta1
      residues 183-188
      <400> 56
Gly Lys Glu Arg Glu Gly
                  5
 1
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<210> 57
     <211> 6
     <212> PRT
     <213> Artificial Sequence
     <220>
     <223> Variant sequence at human heregulin-betal
      residues 183-188
     <400> 57
Thr Asn Ser Arg Glu Gly
                 5
 1
      <210> 58
      <211> 6
      <212> PRT
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      <223> Variant sequence at human heregulin-beta1
      residues 183-188
      <400> 58
Asp Lys Ser Arg Glu Gly
 1
      <210> 59
      <211> 6
      <212> PRT
      <213> Artificial Sequence
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      <223> Variant sequence at human heregulin-beta1
      residues 183-188
      <400> 59
Gly Glu Asp Arg Lys Gln
                 5
 1
      <210> 60
      <211> 6
      <212> PRT
      <213> Artificial Sequence
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<220>
      <223> Variant sequence at human heregulin-beta1
      residues 183-188
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Gly Arg Glu Arg Glu Gly
                 5
      <210> 61
      <211> 5
      <212> PRT
      <213> Homo sapiens
      <400> 61
Val Asn Gly Gly Glu
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      <211> 5
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      <223> Variant sequence at human heregulin-beta1
      residues 191-195
      <400> 62
Val Asn Gly Gly Glu
                 5
 1
      <210> 63
      <211> 5
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      <213> Artificial Sequence
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      residues 191-195
      <400> 63
Val Asn Gly Gly Val
                  5
 1
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      residues 191-195
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Val Asn Gly Gly Gln
 1
      <210> 65
      <211> 5
      <212> PRT
      <213> Homo sapiens
      <400> 65
Phe Met Val Lys Asp
 1
                 5
      <210> 66
      <211> 5
      <212> PRT
      <213> Artificial Sequence
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      <223> Variant sequence at human heregulin-beta1
      residues 197-201
     <400> 66
Tyr Lys Val Arg Ile
 1
      <210> 67
      <211> 5
      <212> PRT
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residues 197-201

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      residues 197-201
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Met Arg Val Arg Thr
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Pro Ser Arg Tyr Leu
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      residues 205-209
      <400> 73
Thr Pro Tyr Leu Met
                 5
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      <210> 74
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Tyr Gly Tyr Leu Met
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      residues 205-209
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Tyr Arg Tyr Arg Met
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      residues 205-209
      <400> 76
Thr His Tyr Arg Gly
                 5
 1
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      residues 205-209
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Thr His Tyr Arg Met
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      residues 205-209
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Tyr Lys Tyr Arg Met
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Thr Lys Tyr Arg Gly
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Tyr Lys Tyr Arg Leu
                 5
 1
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<210> 81
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Lys Cys Pro Asn Glu Phe
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      residues 211-216
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Arg Cys Ser Leu Glu Phe
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Arg Cys Ser Glu Glu Phe
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      residues 211-216
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Lys Cys Pro Lys Glu Met
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Arg Cys Thr Val Glu Tyr
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Arg Cys Thr Val Glu Tyr
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Lys Cys Asn Ser Glu Phe
1
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Arg Cys Lys Lys Glu Phe
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Gln Asn Tyr Val Met
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      residues 222-226
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Gln Trp Tyr Val Ile
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      <210> 91
      <211> 5
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 Ser His Leu Val
 Lys Cys Ala Glu Lys Glu Lys Glu Lys Thr Phe Cys Val Asn

 1
 5
 10
 10
 15
 15

 Gly Gly Glu Cys Phe Met Val Lys Asp Leu Ser Asn Pro Ser Arg Tyr
 20
 25
 30
 30

 Leu Cys Lys Cys Pro Asn Glu Phe Thr Gly Asp Arg Cys Gln Asn Tyr
 35
 40
 45

 Val Met Ala Ser 50
 50
 50
 50
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<400> 93

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Cont

Ile Val Glu Ser Asn Glu Ile Ile Thr Gly Met Pro Ala Ser Thr Glu Gly Ala Tyr Val Ser Ser Glu Ser Pro Ile Arg Ile Ser Val Ser Thr Glu Gly Ala Asn Thr Ser Ser Ser Thr Ser Thr Ser Thr Thr Gly Thr Ser His Leu Val Lys Cys Ala Glu Lys Glu Lys Thr Phe Cys Val Asn Gly Glu Cys Phe Met Val Lys Asp Leu Ser Asn Pro Ser Arg Tyr Leu Cys Lys Cys Pro Asn Glu Phe Thr Gly Asp Arg Cys Gln Asn Tyr Val Met Ala Ser Phe Tyr Lys His Leu Gly Ile Glu Phe Met Glu Ala Glu Glu Leu Tyr Gln Lys Arg Val Leu Thr Ile Thr Gly Ile Cys Ile Ala Leu Leu Val Val Gly Ile Met Cys Val Val Ala Tyr Cys Lys Thr Lys Lys Gln Arg Lys Lys Leu His Asp Arg Leu Arg Gln Ser Leu Arg Ser Glu Arg Asn Asn Met Met Asn Ile Ala Asn Gly Pro His His Pro Asn Pro Pro Pro Glu Asn Val Gln Leu Val Asn Gln Tyr Val Ser Lys Asn Val Ile Ser Ser Glu His Ile Val Glu Arg Glu Ala Glu Thr Ser Phe Ser Thr Ser His Tyr Thr Ser Thr Ala His His Ser Thr Thr Val Thr Gln Thr Pro Ser His Ser Trp Ser Asn Gly His Thr Glu Ser Ile Leu Ser Glu Ser His Ser Val Ile Val Met Ser Ser Val Glu Asn Ser Arg His Ser Ser Pro Thr Gly Gly Pro Arg Gly Arg Leu Asn Gly Thr Gly Gly Pro Arg Glu Cys Asn Ser Phe Leu Arg His Ala Arg Glu Thr Pro Asp Ser Tyr Arg Asp Ser Pro His Ser Glu Arg Tyr Val Ser Ala Met Thr Thr Pro Ala Arg Met Ser Pro Val Asp Phe His Thr Pro Ser Ser Pro Lys Ser Pro Pro Ser Glu Met Ser Pro Pro Val Ser Ser Met

CM

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Thr Val Ser Met Pro Ser Met Ala Val Ser Pro Phe Met Glu Glu Glu
465
                    470
                                         475
Arg Pro Leu Leu Val Thr Pro Pro Arg Leu Arg Glu Lys Lys Phe
                485
                                    490
Asp His His Pro Gln Gln Phe Ser Ser Phe His His Asn Pro Ala His
            500
                                505
                                                     510
Asp Ser Asn Ser Leu Pro Ala Ser Pro Leu Arg Ile Val Glu Asp Glu
                            520
Glu Tyr Glu Thr Thr Gln Glu Tyr Glu Pro Ala Gln Glu Pro Val Lys
                        535
Lys Leu Ala Asn Ser Arg Arg Ala Lys Arg Thr Lys Pro Asn Gly His
                    550
                                        555
Ile Ala Asn Arg Leu Glu Val Asp Ser Asn Thr Ser Ser Gln Ser Ser
                565
                                    570
                                                         575
Asn Ser Glu Ser Glu Thr Glu Asp Glu Arg Val Gly Glu Asp Thr Pro
                                585
Phe Leu Gly Ile Gln Asn Pro Leu Ala Ala Ser Leu Glu Ala Thr Pro
                            600
                                                605
Ala Phe Arg Leu Ala Asp Ser Arg Thr Asn Pro Ala Gly Arg Phe Ser
                        615
                                            620
Thr Gln Glu Glu Ile Gln Ala Arg Leu Ser Ser Val Ile Ala Asn Gln
                                        635
                                                             640
Asp Pro Ile Ala Val
                645
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      <211> 56
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Gly Thr Ser His Leu Val Lys Cys Gly Trp Asp Arg Glu Gly Phe Cys
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Val Asn Gly Glu Cys Phe Met Val Lys Asp Leu Ser Asn Pro Ser
            20
                                25
                                                     30
Arg Tyr Leu Cys Lys Cys Pro Asn Glu Phe Thr Gly Asp Arg Cys Gln
                            40
                                                45
Asn Tyr Val Ile Ala Ser Phe Tyr
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      <210> 95
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<212> PRT

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<213> Homo sapiens
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35 40
Asn Tyr Val Ile Ala Ser Phe Tyr
50 55

<210> 97 <211> 56 <212> PRT

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<400> 97

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<211> 56 <212> PRT <213> Homo sapiens <400> 98 Gly Thr Ser His Leu Val Lys Cys Ala Glu Lys Glu Lys Thr Phe Cys 10 Val Asn Gly Glu Cys Phe Met Val Lys Asp Leu Ser Asn Tyr Arg 20 25 Tyr Arg Met Cys Lys Cys Pro Asn Glu Phe Thr Gly Asp Arg Cys Gln 45 Asn Tyr Val Ile Ala Ser Phe Tyr 50 55 <210> 99 <211> 56 <212> PRT <213> Homo sapiens <400> 99 Gly Thr Ser His Leu Val Lys Cys Ala Glu Lys Glu Lys Thr Phe Cys 10 Val Asn Gly Glu Cys Phe Met Val Lys Asp Leu Ser Asn Thr His 20 Tyr Arg Met Cys Lys Cys Pro Asn Glu Phe Thr Gly Asp Arg Cys Gln 40 Asn Tyr Val Met Ala Ser Phe Tyr 50 55 <210> 100 <211> 56 <212> PRT <213> Homo sapiens <400> 100 Gly Thr Ser His Leu Val Lys Cys Ala Glu Lys Glu Lys Thr Phe Cys Val Asn Gly Gly Glu Cys Phe Met Val Lys Asp Leu Ser Asn Thr Lys 20 25 30 Tyr Arg Gly Cys Lys Cys Pro Asn Glu Phe Thr Gly Asp Arg Cys Gln 40

36

Asn Tyr Val Met Ala Ser Phe Tyr

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Gly Thr Ser His Leu Val Lys Cys Ala Glu Lys Glu Lys Thr Phe Cys
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                                     10
                                                         15
Val Asn Gly Glu Cys Phe Met Val Lys Asp Leu Ser Asn Pro Ser
                                 25
Arg Tyr Leu Cys Lys Cys Pro Asn Glu Phe Thr Gly Asp Arg Cys Gln
        35
                             40
                                                 45
Trp Tyr Val Ile Ala Ser Phe Tyr
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      <210> 102
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      <213> Homo sapiens
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Gly Thr Ser His Leu Val Lys Cys Ala Glu Lys Glu Lys Thr Phe Cys
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                                                         15
Val Asn Gly Glu Cys Phe Met Val Lys Asp Leu Ser Asn Pro Ser
                                25
Arg Tyr Leu Cys Lys Cys Pro Asn Glu Phe Thr Gly Asp Arg Cys Gln
        35
                                                45
His Tyr Val Ile Ala Ser Phe Tyr
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Gly Thr Trp Glu Leu Val Pro Cys Gly Trp Asp Arg Glu Gly Phe Cys
1
Val Asn Gly Glu Cys Phe Met Val Lys Asp Leu Ser Asn Pro Ser
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Arg Tyr Leu Cys Lys Cys Pro Asn Glu Phe Thr Gly Asp Arg Cys Gln

40

35

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Gly Thr Ser His Leu Val Lys Cys Ala Glu Lys Glu Lys Thr Phe Cys
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Val Asn Gly Gly Glu Cys Phe Met Val Lys Asp Leu Ser Asn Tyr Gly
            20
                                25
                                                     30
Tyr Leu Met Cys Lys Cys Pro Asn Glu Phe Thr Gly Asp Arg Cys Gln
                            40
                                                 45
Asn Tyr Val Ile Ala Ser Phe Tyr
    50
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Gly Thr Ser His Leu Val Lys Cys Gly Glu Glu Arg Glu Gly Phe Cys
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Val Asn Gly Gly Glu Cys Tyr Arg Val Lys Thr Leu Ser Asn Pro Ser
            20
                                25
Arg Tyr Leu Cys Lys Cys Pro Asn Glu Phe Thr Gly Asp Arg Cys Gln
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                            40
                                                 45
Asn Tyr Val Met Ala Ser Phe Tyr
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Gly Thr Ser His Leu Val Lys Cys Gly Glu Glu Arg Glu Gly Phe Cys
Val Asn Gly Glu Cys Phe Met Val Lys Asp Leu Ser Asn Tyr Gly
```

Asn Tyr Val Ile Ala Ser Phe Tyr

20

30

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Tyr Leu Met Cys Lys Cys Pro Asn Glu Phe Thr Gly Asp Arg Cys Gln
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                                                 45
Asn Tyr Val Met Ala Ser Phe Tyr
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Gly Thr Ser His Leu Val Lys Cys Gly Glu Glu Arg Glu Gly Phe Cys
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                                     10
                                                         15
Val Asn Gly Gly Glu Cys Tyr Arg Val Lys Thr Leu Ser Asn Tyr Gly
            20
                                 25
Tyr Leu Met Cys Lys Cys Pro Asn Glu Phe Thr Gly Asp Arg Cys Gln
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                             40
                                                 45
Asn Tyr Val Met Ala Ser Phe Tyr
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Gly Thr Ser His Leu Val Lys Cys Gly Glu Glu Arg Glu Gly Phe Cys
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                                     10
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Val Asn Gly Gly Glu Cys Phe Met Val Lys Asp Leu Ser Asn Pro Ser
Arg Tyr Leu Cys Lys Cys Pro Asn Glu Phe Thr Gly Asp Arg Cys Gln
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                             40
                                                 45
Asn Tyr Val Ile Ala Ser Phe Tyr
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                        55
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Gly Thr Ser His Leu Val Lys Cys Ala Glu Lys Glu Lys Thr Phe Cys
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                                     10
                                                         15
 1
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Val Asn Gly Gly Glu Cys Tyr Arg Val Lys Thr Leu Ser Asn Tyr Gly
                                                     30
            20
                                25
Tyr Leu Met Cys Lys Cys Pro Asn Glu Phe Thr Gly Asp Arg Cys Gln
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Asn Tyr Val Met Ala Ser Phe Tyr
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Gly Thr Ser His Leu Val Lys Cys Ala Glu Lys Glu Lys Thr Phe Cys
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Val Asn Gly Gly Glu Cys Tyr Arg Val Lys Thr Leu Ser Asn Tyr Gly
            20
                                 25
Tyr Leu Met Cys Lys Cys Pro Asn Glu Phe Thr Gly Asp Arg Cys Gln
                            40
                                                 45
Asn Tyr Val Ile Ala Ser Phe Tyr
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      <210> 111
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Gly Thr Ser His Leu Val Lys Cys Ala Glu Lys Glu Lys Thr Phe Cys
Val Asn Gly Gly Glu Cys Tyr Arg Val Lys Thr Leu Ser Asn Pro Ser
            20
                                 25
                                                     30
Arg Tyr Leu Cys Lys Cys Pro Asn Glu Phe Thr Gly Asp Arg Cys Gln
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                            40
Asn Tyr Val Ile Ala Ser Phe Tyr
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      <210> 112
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Gly Thr Ser His Leu Val Lys Cys Gly Glu Glu Arg Glu Gly Phe Cys
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                                    10
Val Asn Gly Glu Cys Tyr Arg Val Lys Thr Leu Ser Asn Pro Ser
                                25
Arg Tyr Leu Cys Lys Cys Pro Asn Glu Phe Thr Gly Asp Arg Cys Gln
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                                                45
Asn Tyr Val Ile Ala Ser Phe Tyr
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      <210> 113
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Gly Thr Ser His Leu Val Lys Cys Gly Glu Glu Arg Glu Gly Phe Cys
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Val Asn Gly Glu Cys Phe Met Val Lys Asp Leu Ser Asn Tyr Gly
                                25
Tyr Leu Met Cys Lys Cys Pro Asn Glu Phe Thr Gly Asp Arg Cys Gln
                                                45
Asn Tyr Val Ile Ala Ser Phe Tyr
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Gly Thr Ser His Leu Val Lys Cys Gly Glu Glu Arg Glu Gly Phe Cys
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                                                        15
Val Asn Gly Glu Cys Tyr Arg Val Lys Thr Leu Ser Asn Tyr Gly
                                25
Tyr Leu Met Cys Lys Cys Pro Asn Glu Phe Thr Gly Asp Arg Cys Gln
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                            40
                                                45
Asn Tyr Val Ile Ala Ser Phe Tyr
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<213> Homo sapiens

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Gly Thr Ser His Leu Val Lys Cys Ala Glu Lys Glu Lys Thr Phe Cys
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Val Asn Gly Glu Cys Tyr Arg Val Lys Thr Leu Ser Asn Tyr Gly 20 25

Tyr Leu Met Cys Lys Cys Pro Asn Glu Phe Thr Gly Asp Arg Cys Gln 40 45

His Tyr Val Ile Ala Ser Phe Tyr 50 55

<210> 116

<400> 115

<211> 56

<212> PRT

<213> Homo sapiens

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Val Asn Gly Glu Cys Tyr Arg Val Lys Thr Leu Ser Asn Tyr Gly 20 25

Tyr Leu Met Cys Lys Cys Pro Asn Glu Phe Thr Gly Asp Arg Cys Gln 45

His Tyr Val Ile Ala Ser Phe Tyr

50